

Amendments to the Specification

Please replace the paragraph beginning on page 50, line 24 with the following amended paragraph:

Co-administration of DT and a control DNA sequence (SEQ ID NO:1; CpG2: *TCCAATGAGCTTCCTGAGTCT*) failed to induce a detectable rise in the anti-DT titers. In contrast, addition of a DNA sequence containing an unmethylated CpG dinucleotide flanked by two 5' purines and two 3' pyrimidines (SEQ ID NO:2; CpG1 (immunostimulatory DNA): *TCCATGACCGTTCTGACGTT*) resulted in a detectable increase in the serum anti-DT IgG titer in 5 of 5 animals. Thus it appears that bacterial DNA containing appropriate motifs such as CPGs (6 KD) can be used as adjuvant to enhance delivery of antigen through the skin for induction of antigen specific antibody responses.

Please replace the paragraph beginning on page 52, line 5 with the following amended paragraph:

The transcutaneous effect of transcutaneous immunization can also be detected by T-cell proliferation. BALB/c mice 6 to 8 weeks of age were shaved and anesthetized as described above for the "immunization procedure". On the day of immunization the backs of the mice were wiped with isopropanol. After the alcohol had evaporated (approximately 5 minutes), 100 μ l of phosphate buffered saline (PBS) containing 100 μ g of DNA (CpG1 or CpG2) and 100 μ g of diphtheria toxoid (DT) was applied to the back for 90 to 120 minutes. Oligonucleotides were synthesized by Oligos Etc with a phosphorothioate backbone to improve stability. Removal of excess antigen was conducted as described in the "immunization procedure." The immunization was repeated 4 and 8 weeks later. Twelve weeks after the primary immunization draining (inguinal) LNs were removed and pooled from five immunized animals. The capacity to proliferate in response to media or antigen (DT) was assessed in a standard 4 day proliferation assay using 3-H incorporation as a readout. The results are shown in Table 7B. Co-administration of DT and a DNA sequence containing an unmethylated CpG dinucleotide

flanked by two 5' purines and two 3' pyrimidines (SEQ ID NO:2 ~~CpG1 (immunostimulatory DNA):~~ *TCCATGACGTTCTGACGTT*) resulted in a detectable increase in the antigen specific proliferative response. Thus it appears that bacterial DNA containing appropriate motifs can be used as adjuvant to enhance delivery of antigen through the skin for induction of proliferative responses.

Please replace the paragraph beginning on page 59, line 22 with the following amended paragraph:

Co-administration of SLA and CpG1 (immunostimulatory DNA containing an unmethylated CpG dinucleotide flanked by two 5' purines and two 3' pyrimidines - SEQ ID NO:2 *TCCATGACGTTCTGACGTT*) or CT resulted in a detectable increase in the antigen specific proliferative response. However, the antigen (SLA) specific proliferative response was approximately 20 times higher in lymph node cell cultures from animals exposed simultaneously to both CpG1 and CT as compared to cultures derived from animals exposed to either adjuvant alone. Thus it appears that bacterial DNA containing appropriate motifs synergizes with ADP ribosylating exotoxins such as CT as adjuvants on the skin to induce higher immune responses than to either adjuvant alone.